

### **REMARKS**

Applicants respectfully request entry of this Amendment and reconsideration of the outstanding objections and rejections of the claims in the above-identified application.

Applicants have amended claims 43-52 in response to the Examiner's objection and to clarify the subject matter of the claims. The amended claims are supported throughout the specification including at page 10, line 11 to page 11, line 10. Applicants submit that the amended claims do not represent new matter.

#### **Objection to Claims**

The Examiner objected to claims 47 and 48 because of word misspellings. Applicants have amended the claims to correct word misspellings. Applicants request withdrawal of the objection of the claims.

#### **Objection to Specification**

The Examiner objected to the specification for referring to canceled claims and for lack of identification of SEQ ID NO:s. Applicants have amended the specification to add SEQ ID NO:s and to correct the reference to the claims. Applicants request withdrawal of the objection of the specification.

#### **Claim Rejections under 35 USC § 112**

The Examiner rejected claims 43-52 as being indefinite. Concerning the term "variants thereof", the Examiner objects that this term is indefinite and could comprise a protein with 0-4 globin chains. Applicants respectfully disagree.

Applicants have amended the claims to recite "variants of the said polypeptide chain". Variants of the proteins are well defined in the specification (page 6, lines 3 to 21) as the protein component, and particularly of alpha or beta globin, having an amino acid sequence which distinguishes itself in relation to the natural sequence by one or more amino acid substitutions, deletions or insertions. In the specification, the variants exhibit at least 90% homology or

identity with the natural sequence. The term "variant" also includes fragments of polypeptide chains, having a length of at least 90% of the parent molecule, for example of alpha and beta globin in the specification. The variants conserve the biological and immunological properties of the parent molecule. Applicants submit, therefore, that the term "variants" is definite under 35 USC § 112.

The Examiner also objects to the phrase "having the capacity to reversibly bind oxygen" in claim 43. The Examiner asserts it is unclear if there are upper and lower limits of reversibly binding ability implied by such terminology. Applicants respectfully traverse this rejection. Claim 43 recites a recombinant hemin protein having the capacity to reversibly bind oxygen. In the specification at page 5, lines 17-21, myoglobin and hemoglobin are identified as hemin proteins whose main function is the reversible binding of oxygen. Applicants submit it is well known in the art that these molecules are characterized by their ability to reversibly bind oxygen. Applicants submit that they do not need to specify the upper and lower limits in order for one of skill in the art to understand what is meant by "reversibly bind". Withdrawal of this rejection is therefore respectfully requested.

The Examiner also objected to the phrase "tile pyrole rings" in claim 44. Amended claim 44 does not recite "tile pyrole rings."

Finally, the Examiner asserted it is unclear if the N-terminal signal peptide of claim 46 is in combination with a vacuolar targeting signal. Applicants have amended claim 46 for clarification.

Applicants assert that claims 43-52 are definite under 35 USC § 112, and withdrawal of these rejections is respectfully requested.

#### **Oath Declaration**

The Examiner objected to the declaration as allegedly being signed by one inventor only. Applicants respectfully disagree. On October 18, 2001, Applicants submitted declarations signed by all 8 inventors. Applicants hereby resubmit copies of the signature pages of the Declaration. Applicants assert it is permissible to submit separate, multiple declarations that are signed by one or more inventors, as long as each inventor has signed at least one of the

declarations. Withdrawal of this objection is respectfully requested.

**Claim Rejections under 35 USC § 102**

The Examiner rejects Claims 43-46 and 48, 49, 51 and 52 as being anticipated by Dieryck et al. Applicants respectfully traverse this rejection.

As with the parent application No. 08/983,564, now granted as U.S. 6,344,600 B1, the present application benefits from the priority claim of French application N FR 95 08615, filed in July 17, 1995, by the same inventors. The PCT extension, PCT/FR96/01123, was filed in July 17, 1996, published as W097/04115. The Examiner has acknowledged the claim for priority.

Applicants call the Examiner's attention to Dieryck et al.'s publication date of December 1995. Applicants hereby submit email correspondence establishing the date of publication of the reference. (copy attached) Since this date is after Applicants' priority date of July 17, 1995, Applicants submit that it is not proper prior art under 35 USC § 102. Applicants submit, therefore, that claims 43-46 and 48, 49, 51 and 52 are patentable over Dieryck et al. Withdrawal of this rejection is requested.

**Claim Rejections under 35 USC § 103**

Claims 43, 45 and 47 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Dieryck et al.

Dieryck et al. is not prior art in view of the claim to the French priority date as explained above. Claims 43, 45, and 47 are therefore patentable over Dieryck et al. under 35 USC § 103. Withdrawal of this rejection is requested.

Claims 43 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dieryck et al. in view of Garlick et al (U.S. 5,521,154). Applicants respectfully traverse this rejection.

Claims 43 and 50 recite a recombinant heme protein comprising at least one iron-containing porphyrin nucleus of plant origin, and a protein component comprising at least one polypeptide chain of animal origin.

As discussed above, Dieryck et al. is not proper prior art over the present invention. Applicants submit that the remaining Garlick et al. reference does not describe a recombinant heme protein comprising at least one iron-containing porphyrin nucleus of plant origin, and a

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protein component comprising at least one polypeptide chain of animal origin. Rather, Garlick et al. describe a method for purifying hemoglobin and cross-linking hemoglobin from blood cells after collecting mammalian blood, separating red blood cells from the collected blood and lysing the red blood cells. The teaching of Garlick et al. is based on extraction and purification of native hemoglobin, and on cross-linking of this native hemoglobin with a chemical agent. The effects of such modification are to improve stability of native hemoglobin to autoxidation.

Garlick et al., however, nowhere teaches or suggests a recombinant heme protein comprising a porphyrin nucleus of plant origin and a polypeptide chain of animal origin. Applicants submit, therefore, that Garlick et al. does not teach all elements of claims 43 and 50. Nor does Garlick et al. provide any motivation or suggestion to modify its disclosure to provide heme proteins having all elements of claims 43 and 50. Claims 43 and 50 are therefore patentable over the cited references. Withdrawal of the rejection is requested.

#### SUMMARY

Applicants submit that all pending claims are in condition for allowance and notification to that effect is earnestly solicited. Should the Examiner consider that the arguments presented here require further clarification or discussion, the Applicant hereby requests a personal interview with the Examiner and her Supervisor. The Examiner is invited to contact Applicants' representative if prosecution may be assisted thereby.

Respectfully submitted,

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